*Original Report*

# *Staphylococcus aureus* bacteremic pneumonia: differences between community and nosocomial acquisition

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**Objective:** The aim of the study was to ascertain the clinical and epidemiologic characteristics of patients with nosocomial or community-acquired *Staphylococcus aureus* bacteremic pneumonia.

**Methods:** A prospective study of 134 cases diagnosed between January 1990 and December 1995 was performed.

**Results:** Fifty cases involved primary bacteremic pneumonias, of which 80% were nosocomial (the majority, 72%, in intensive care unit patients, of whom 57% were post-surgery). Of the 84 cases of secondary pneumonia, 36 were non-intravenous drug users (78% nosocomial, of whom 43% were in the intensive care unit), and 48 cases were intravenous drug users (98% community-acquired).

**Conclusions:** Nosocomial *S. aureus* bacteremic pneumonia was especially frequent in intensive care unit patients (68.1%), and community-acquired pneumonia in intravenous drug users (72.3%). In non-intravenous drug users, clinical outcome and mortality were similar for nosocomial and community-acquired pneumonia.

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## INTRODUCTION

*Staphylococcus aureus* is an important cause of severe pulmonary infection.[1–4] Community-acquired *S. aureus* pneumonia has been reported as being associated with influenza,[5–8] with cystic fibrosis in children,[9] and with intravenous drug use.[10–12] Nosocomial pneumonia has been reported in patients with severe underlying illnesses,[1,13] in burns unit patients,[14] and, more recently, in patients in intensive care and receiving mechanical ventilation.[15,16]

The clinical manifestations of staphylococcal pneumonia do not seem to differ from other bacterial etiologies.[2,17,18] They have a heterogeneous radiologic pattern,[17–21] with frequent cavitation[17,19,22] and high mortality.[1–4,17]

However, since the publication in 1919[5] of the first paper on staphylococcal pneumonia, there have been few prospective studies[23] that have included comprehensive series on this subject. In this study, we include 134 cases of bacteremic pneumonia caused by *S. aureus* diagnosed over a period of 6 years, with the aim of describing the clinical and epidemiologic characteristics of this infection.

## PATIENTS AND METHODS

### Hospital

The Hospital Universitario San Carlos (HUSC) is a tertiary-care center with 1479 beds, serving a population of 570 000 inhabitants in the northwest of the Madrid metropolitan area.

### Microbiological methods

Samples for microbiological diagnosis were taken using bronchial aspiration, bronchoalveolar lavage, and protected brush catheter. The Murray and Washington criteria[24] were used to evaluate the quality of these samples, in order to rule out those with high levels of oropharyngeal contamination. We considered as significant for the diagnosis of pneumonia the finding of *S. aureus* in pure culture in two samples from the same patient taken on consecutive days. Protected brush catheter samples were obtained using the technique described by Wimberley et al.[25] We considered colony counts of $\geq 10^3$ CFU/mL of *S. aureus* to be significant. Bronchoalveolar lavage samples were also obtained by bronchoscopy. When they arrived at the laboratory, a quantitative culture was taken,[26] and an *S. aureus* count of $10^5$ CFU/mL was considered significant.

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Blood cultures were processed using the BACTEC-NR 660 system until April 1992, and BACTEC-NR 860 thereafter.

### Study population and design

The study included those patients with *S. aureus* pneumonia who also met the criteria for the diagnosis of significant *S. aureus* bacteremia between 1 January 1990 and 31 December 1995. For study purposes, bacteremic pneumonia was divided into three groups: primary pneumonia, secondary pneumonia in intravenous drug users (IVDUs), and secondary pneumonia in non-IVDUs. A prospective evaluation was made, and a comparison was made of the epidemiologic and clinical characteristics of the patients who acquired pneumonia in the hospital and in the community in each of the three groups.

### Definition of terms

Staphylococcal pneumonia: a diagnosis was made when there were symptoms of infection of the lower respiratory tract and pulmonary infiltrates in the chest X-ray not attributable to other causes, coinciding with the isolation of *S. aureus* as the only pathogen in two samples of bronchial aspirate taken on consecutive days or in one or more of the following samples: protected brush catheter, bronchoalveolar lavage, and/or blood culture.

*S. aureus* bacteremia: one or more positive blood cultures for this microorganism.

Bacteremic pneumonia: patient with significant bacteremia and pneumonia according to the above definitions.

Primary pneumonia:[27–30] clinical symptoms and signs of lower respiratory tract infection, and the isolation of *S. aureus* in respiratory samples preceding or coinciding with the diagnosis of staphylococcal bacteremia.

Secondary pneumonia: when its clinical manifestations appeared in the evolution of a patient previously diagnosed with *S. aureus* bacteremia.[18]

Aspiration pneumonia was defined following the criteria of Finegold.[31]

Nosocomial pneumonia: clinical manifestations began within 72 h after admission to hospital, and a sample positive for *S. aureus* was taken during this period.

Community-acquired pneumonia: a positive sample (respiratory and/or blood cultures) was obtained before the first 72 h after admission, and the patient had not been admitted in the previous 2 weeks.

Predisposing factors: invasive procedures or treatments that favored the acquisition of infection.

Respiratory distress: following the clinical definition by Kollef and Schuster.[32]

Death was considered to be due to the staphylococcal infection when one or more of the following criteria were fulfilled: a culture which was positive for *S. aureus* at the time of death (blood culture or representative sample from the lower respiratory tract); persistent respiratory symptoms and radiologic evidence of the persistence of pneumonia; and death with no other explanation within the first 7 days after the diagnosis of staphylococcal pneumonia. Deaths not explained by these criteria were considered to result from the patient's underlying disease.

### Statistical analysis

Analysis of the variables was carried out using the statistical program BMDP V7.0 for Unix. The Mann–Whitney test was used for comparison of the quantitative data. Qualitative variables were associated using the chi-square test, and when the conditions of validity of this test were not met, Fisher's exact test was used. Results were considered statistically significant when $P \leq 0.05$.

## RESULTS

### General data

One hundred and thirty-four cases of bacteremic staphylococcal pneumonia were analyzed and classified as follows: primary pneumonia (50 episodes, 37.3%); secondary pneumonia in IVDUs (48 episodes, 35.8%); and secondary pneumonia in non-IVDUs (36 episodes, 26.9%). There were 69 (51.5%) cases of nosocomial bacteremic pneumonia (68.1% in intensive care units (ICUs)) and 65 (48.5%) cases of community-acquired bacteremic pneumonia (72.3% IVDUs).

### Primary pneumonia

Of the 50 cases of primary pneumonia, 40 (80%) were nosocomial, and 10 (20%) community-acquired.

There were significant differences between patients with nosocomial primary pneumonia and those with community-acquired primary pneumonia with regard to methicillin-resistant *Staphylococcus aureus* (MRSA) infection, area of admission, age, length of hospital stay, and the following predisposing factors: history of food aspiration, previous stay in the ICU, previous surgery, previous intubation, and insertion of a nasogastric tube. Table 1 shows a comparison of the age, area of admission and predisposing factors for infection in patients with primary pneumonia acquired both in the community and in the hospital.

The most frequent underlying diseases in patients with nosocomial and community-acquired primary bacteremic pneumonia are shown in Table 2.

With regard to complications, no significant differences were found between patients with nosocomial pneumonia and those with community-acquired pneumonia (Table 2).

**Table 1.** Age, area of admission and predisposing factors of patients with nosocomial or community-acquired bacteremic primary pneumonia

| | *Nosocomial primary pneumonia (n=40)* | *Community-acquired primary pneumonia (n=10)* | *P-value* |
|---|---|---|---|
| MRSA pneumonia | 19 (47.5%) | 2 (20%) | 0.16 |
| Age (average) | 56.4±23.7 | 74.8±18.8 | 0.03 |
| Hospital stay (average) | 37.9±24.9 | 19.3±9.5 | 0.01 |
| Area of admission | | | |
| ICU and post-surgical recovery | 29 (72.5%) | 1 (10%) | <0.01 |
| Internal medicine | 8 (20%) | 9 (90%) | <0.01 |
| Surgery | 3 (7.5%) | 0 | 1 |
| Predisposing factors | | | |
| Antibiotics/predisposing factors | 9 (22.5%) | 1 (10%) | 1 |
| Previous pneumonia | 4 (10%) | 0 | 0.79 |
| Neutropenia | 0 | 1 (10%) | 0.2 |
| Aspiration | 4 (10%) | 8 (80%) | <0.01 |
| Previous ICU stay | 31 (77.5%) | 0 | <0.01 |
| Intubation | 31 (77.5%) | 0 | <0.01 |
| Nasogastric tube | 34 (85%) | 1 (10%) | <0.01 |
| Altered mental state | 35 (87.5%) | 5 (50%) | 0.01 |
| Previous surgery | 23 (57.5%) | 0 | <0.01 |
| Dialysis | 2 (5%) | 0 | 1 |
| Transfusion | 7 (17.5%) | 0 | 0.3 |

MRSA, methicillin-resistant *S. aureus*.

**Table 2.** Underlying diseases and clinical outcome of patients with nosocomial or community-acquired bacteremic primary pneumonia

| | *Nosocomial primary pneumonia (n=40)* | *Community-acquired primary pneumonia (n=10)* | *P-value* |
|---|---|---|---|
| Underlying diseases | | | |
| Underlying diseases (average) | 1.5±1.2 | 1.7±0.6 | 0.6 |
| Lung diseases | 7 (17.5%) | 1 (10%) | 1 |
| Diabetes mellitus | 5 (12.5%) | 1 (10%) | 1 |
| Heart disease | 5 (12.5%) | 2 (20%) | 1 |
| Vascular disease | 2 (5%) | 0 | 1 |
| Liver disease | 4 (10%) | 0 | 0.79 |
| Neoplasia | 7 (17.5%) | 1 (10%) | 1 |
| Cerebrovascular accident | 10 (25%) | 3 (30%) | 1 |
| Arterial hypertension | 7 (17.5%) | 2 (20%) | 1 |
| Chronic renal insufficiency | 2 (5%) | 0 | 1 |
| Clinical outcome | | | |
| Respiratory distress | 15 (37.5%) | 4 (40%) | 1 |
| Septic shock | 16 (40%) | 3 (30%) | 1 |
| DIC | 2 (5%) | 0 | 1 |
| Neurologic alterations | 7 (17.5%) | 1 (10%) | 1 |
| Mortality due to infection | 21 (52.5%) | 3 (30%) | 0.29 |

DIC, disseminated intravascular coagulation.

Mortality due to the staphylococcal infection was 48%, and was higher in the group of patients with nosocomially acquired pneumonia than in patients with community-acquired pneumonia (52.5% versus 30%; P=0.29).

## Secondary pneumonia

**Secondary pneumonia in IVDUs.** Of the 84 cases of secondary pneumonia studied, 48 (57.1%) involved IVDUs. Of these, 47 (97.9%) acquired the infection in the community, and only one patient had secondary nosocomial pneumonia. This was a 22-year-old male who was admitted with deep venous thrombosis and who, at 10 days, developed bacteremia due to methicillin-susceptible *S. aureus*, and pneumonia with a nodular image on the upper left lobe. Treatment was begun with vancomycin; the patient improved, and, after 10 days of treatment, he requested voluntary discharge.

**Community-acquired secondary pneumonia in IVDUs.** This infection affected young people, mainly men, and was due to MRSA in four patients (8.5%). In addition to intravenous drug use, the predisposing factors for infection (Table 3) were previous infection (25.5%), previous pneumonia (10.6%), or previous antibiotic treatment (17%).

With regard to underlying diseases (Table 3), of the 47 patients studied, 35 (74.5%) had HIV infection.

**Table 3.** Secondary pneumonia in intravenous drug users (IVDUs)

| | *Community-acquired secondary pneumonia in IVDUs (n=47)* |
|---|---|
| MRSA infection | 4 (8.5%) |
| Age (average) | 27.2±4 |
| Internal medicine | 47 (100%) |
| Predisposing factors | |
| Previous infection | 12 (25.5%) |
| Previous antibiotherapy | 8 (17%) |
| Previous pneumonia | 5 (10.6%) |
| Neutropenia | 1 (2.1%) |
| Alcoholism | 2 (4.2%) |
| Endovascular catheter | 2 (4.2%) |
| Underlying diseases | |
| HIV infection | 35 (74.5%) |
| Liver disease | 4 (8.5%) |
| Clinical outcome | |
| Respiratory distress | 3 (6.4%) |
| Septic shock | 9 (19.1%) |
| DIC | 5 (10.6%) |
| Neurologic alterations | 4 (8.5%) |
| Mortality due to infection | 9 (19.1%) |

MRSA, methicillin-resistant *S. aureus*; HIV, human immunodeficiency virus; DIC, disseminated intravascular coagulation.

The complications suffered by these patients are shown in Table 3. Mortality due to infection was lower than in the other groups studied (19.1%).

### Secondary pneumonia in non-IVDUs

Of the 36 non-IVDU cases with secondary pneumonia, 28 (77.8%) were nosocomial in origin and eight (22.2%) were community-acquired.

In the group of patients with nosocomial pneumonia, a higher proportion of the infections was due to MRSA, infection was especially frequent in the ICU, and the patients had a higher average age. Table 4 shows and compares the predisposing factors for both groups of patients.

Among patients with nosocomial pneumonia, 11 (39.3%) had lung diseases, and 11 (39.3%) had neoplasia. In the case of patients with community-acquired pneumonia, the most common underlying condition was neoplasia (37.5%).

With regard to complications, there was no significant difference between nosocomial and community-acquired infections (Table 5).

Mortality due to staphylococcal infection was 47.2%, and was higher in patients with nosocomial pneumonia than in patients with community-acquired pneumonia (53.6% versus 25%, P=0.24).

## DISCUSSION

*S. aureus* pneumonia is a clinical entity with high morbidity and mortality.[1–4,17] Together with endovascular catheters and cutaneous infection, it is reported to be one of the most common portals of entry for bacteremia,[29,33] and it appears frequently as a secondary or metastatic infection.[28,33]

We found 69 cases (51.5%) of nosocomial pneumonia (58% primary) and 65 (48.5%) community-acquired cases (15.3% primary). The proportion of nosocomial pneumonia would increase to 79% if we excluded IVDUs. These data agree with the literature.[1,2,20]

The patients with community-acquired pneumonia included in our analysis fall into the following groups:

**Table 4.** Age, area of admission and predisposing factors for infection in non-IVDU patients with nosocomial or community-acquired pneumonia

| | *Nosocomial secondary pneumonia in non-IVDUs (n=28)* | *Community-acquired secondary pneumonia in non-IVDUs (n=8)* | *P-value* |
|---|---|---|---|
| MRSA pneumonia | 11 (39.3%) | 0 | 0.07 |
| Age (average) | 65.8±16 | 49.8±27.8 | 0.12 |
| Hospital stay (average) | 39.8±27.1 | 28.8±24.1 | 0.20 |
| Area of admission | | | |
| ICU and post-surgical recovery | 12 (42.9%) | 0 | 0.03 |
| Internal medicine | 13 (46.4%) | 8 (100%) | 0.01 |
| Surgery | 3 (10.7%) | 0 | 1 |
| Predisposing factors | | | |
| Previous antibiotherapy | 6 (21.4%) | 1 (12.5%) | 1 |
| Previous pneumonia | 0 | 1 (12.5%) | 0.22 |
| Neutropenia | 3 (10.7%) | 1 (12.5%) | 1 |
| Aspiration | 1 (3.6%) | 0 | 1 |
| Previous ICU stay | 16 (57.1%) | 0 | <0.01 |
| Intubation | 17 (60.7%) | 0 | <0.01 |
| Nasogastric tube | 16 (57.1%) | 0 | <0.01 |
| Altered mental state | 10 (35.7%) | 1 (12.5%) | 0.38 |
| Previous surgery | 14 (50%) | 0 | 0.01 |
| Chemotherapy | 7 (25%) | 3 (37.5%) | 0.65 |
| Dialysis | 0 | 1 (12.5%) | 0.22 |
| Transfusion | 14 (50%) | 0 | 0.01 |
| Central catheter | 24 (85.7%) | 4 (50%) | 0.05 |
| Urinary catheter | 23 (82.1%) | 1 (12.5%) | <0.01 |

MRSA, methicillin-resistant *S. aureus*; ICU, intensive care unit.

**Table 5.** Underlying diseases and clinical outcome of non-IVDU patients with community-acquired or nosocomial pneumonia

| | *Nosocomial secondary pneumonia in non-IVDUs (n=28)* | *Community-acquired secondary pneumonia in non-IVDUs (n=8)* | *P-value* |
|---|---|---|---|
| Underlying diseases | | | |
| Underlying diseases (average) | 2.4±1.2 | 1.6±1.1 | 0.12 |
| Lung diseases | 11 (39.3%) | 1 (12.5%) | 0.22 |
| Diabetes mellitus | 3 (10.7%) | 1 (12.5%) | 1 |
| Heart diseases | 11 (39.3%) | 1 (12.5%) | 0.22 |
| Vascular diseases | 3 (10.7%) | 0 | 1 |
| Liver diseases | 3 (10.7%) | 0 | 1 |
| Neoplasias | 11 (39.3%) | 3 (37.5%) | 1 |
| Cerebrovascular accident | 5 (17.9%) | 1 (12.5%) | 1 |
| Arterial hypertension | 8 (28.6%) | 1 (12.5%) | 0.64 |
| Chronic renal insufficiency | 1 (3.6%) | 1 (12.5%) | 0.4 |
| Clinical outcome | | | |
| Respiratory distress | 8 (28.6%) | 3 (37.5%) | 0.67 |
| Septic shock | 11 (39.3%) | 2 (25%) | 0.68 |
| DIC | 0 | 0 | |
| Neurologic alterations | 6 (21.4%) | 2 (25%) | 1 |
| Mortality due to infection | 15 (53.6%) | 2 (25%) | 0.24 |

DIC, disseminated intravascular coagulation.

(1) IVDUs with pneumonia probably caused by septic emboli (72.3%); (2) patients with secondary pneumonia and severe underlying illnesses (15.3%), mainly neoplasia and chronic renal insufficiency; and (3) elderly patients with altered mental states and aspiration pneumonia (12.3%). In this sense, we differ on several points from the study by Woodhead et al,[34] which reviewed 61 cases of community-acquired staphylococcal pneumonia. The authors found that a high percentage of their patients suffered from chronic conditions (lung diseases), and that influenza virus infection was an important factor associated with pneumonia. We did not find any cases associated with the influenza virus. We can attribute this difference to greater use of the influenza vaccine in certain population groups (elderly and chronically ill patients), and to the generalized use of antibiotics in the treatment of community-acquired respiratory processes. On the other hand, the number of cases of staphylococcal pneumonia associated with the influenza virus reported by Woodhead et al and other previous studies could be skewed by imprecise diagnostic considerations.

Most of our patients with community-acquired pneumonia were IVDUs (72.3%), and they had pneumonia with a favorable clinical outcome. Of the IVDU group, the majority (93.6%) had septic emboli as a result of tricuspid endocarditis. This has been previously reported by other authors.[10–12] It is interesting that four of these patients (8.5%) were infected by MRSA. This could lead us to consider this population as a route for disseminating this microorganism in the community, as described by Saravolatz in 1987.[35] On the other hand, half of our group of aged patients with community-acquired aspiration pneumonia suffered from an altered mental state. None of these patients came from a nursing home. The greatest frequency of community-acquired staphylococcal pneumonia has been reported among patients who live in these centers.[20,36–38] However, given our results, we consider advanced age and associated characteristics (altered mental state in most cases) as the determining risk factor in this group regardless of whether the infection was acquired in these centers.

As was the case with other authors,[1,2,17,20,21,39] we can also state that *S. aureus* pneumonia is mainly nosocomial. In general, most of our patients developed pneumonia in the ICU (72.5% of primary nosocomial cases and 42.8% of secondary cases in non-IVDU nosocomial patients). Another risk group comprised elderly patients with a high number of underlying illnesses, mainly pulmonary illnesses or neoplasia. These patients were especially prone to secondary pneumonia, and represented 26% of all cases of nosocomially-acquired pneumonia. The remaining patients (7.3%) were over 85 years of age, with altered mental status and aspiration pneumonia during their stay in hospital for other reasons.

At present, nosocomial staphylococcal pneumonia is reported in ICU patients, patients undergoing intubation and mechanical ventilation, very often in young people with multiple traumas, and especially in post-surgical patients. Our study agrees with these reports; 59.4% of all cases of nosocomial pneumonia developed in the ICU, and 68.1% had a previous stay in the ICU, although not all of them developed the infection in this area. This figure is greater than that found in the study by Musher et al.[2] The many studies on ICU pneumonia in recent years reveal the importance of the role of *S. aureus*.[15,16,40–42]

The clinical manifestations of staphylococcal pneumonia[2,17,21] do not seem to differ from other bacterial etiologies. There can be a fulminant and acute course in some cases,[20] and a subacute course in others.[43,44] Our patients generally presented acute clinical forms, and a frequency of complications similar to that reported for pneumonia due to Gram-negative bacilli.[39]

In our study, we found a high frequency of MRSA pneumonia (26%), but this varied according to the groups studied, in such a way that the greatest proportion of MRSA pneumonia was found in nosocomial primary pneumonia (47.5%), followed by nosocomial secondary pneumonia in non-IVDUs (39.3%). In community-acquired primary pneumonia the frequency was 20%, and in secondary pneumonia in IVDUs it was 8.3%. The frequency of MRSA pneumonia varies from study to study, according to the population groups analyzed.[2,20] In general, MRSA pneumonia is nosocomial in origin,[3,8,13] and there are no extensive studies (few large series of patients) clarifying its incidence in the community.[44] However, some community-acquired cases are included in series of staphylococcal pneumonia,[13] in many cases associated with infections in nursing homes[37] or community-acquired MRSA bacteremia in IVDUs.[35,45]

The mortality due to staphylococcal pneumonia in the pre-antibiotic era varied between 50% and 90%.[5,46] Despite adequate antibiotic therapy, mortality is still high, at around 30–50%.[1–4,17] In our study, we found a high mortality rate (48% in primary pneumonia, and 47.2% in non-IVDU secondary pneumonia), except in drug users (19.1%). These figures are closer to those for pneumonia caused by Gram-negative bacilli, and are greater than those for pneumonia caused by other Gram-positive microorganisms.[39]

## CONCLUSION

In our study population, staphylococcal pneumonia appeared as a severe infection, frequently associated with clinical complications and a high mortality rate. Nosocomial *S. aureus* bacteremic pneumonia was frequently due to MRSA, and was especially frequent in ICUs. Most of our patients with community-acquired pneumonia were IVDUs.

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